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09/603,208	06/23/2000	Markus Pompejus	BGI-124CP	9692

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LAHIVE & COCKFIELD
28 STATE STREET
BOSTON, MA 02109

EXAMINER

SPIEGLER, ALEXANDER H

ART UNIT	PAPER NUMBER
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1637

DATE MAILED: 02/08/2002

7

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/603,208

Applicant(s)

POMPEJUS ET AL.

Examiner

Alexander H. Spiegler

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~~1636~~ 1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 October 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-38 is/are pending in the application.
- 4a) Of the above claim(s) 18-35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-17 and 36-38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: CRF Errors Corrected by STIC Systems Branch.

DETAILED ACTION

Election/Restrictions

1. This action is response to the election without traverse of Group I (claims 1-17 and 36-38, SEQ ID NO: 1) in Paper No. 6, filed on October 25th, 2001.

Despite the election *without* traverse, applicant provides arguments traversing the restriction requirement of Paper No. 5. In particular, applicant argues that ten nucleic acid sequences should be searched, as searching up to ten nucleic acid sequences does not constitute a serious burden on the examiner.

These arguments have been fully considered but are not persuasive as each sequence is patentably distinct, as they are unrelated sequences (i.e. sequences with a different genetic makeup, therefore having different chemical structures) and for the reasons of record. Therefore, this restriction requirement is made FINAL.

The claims should be amended to recite the claimed nucleic acid, SEQ ID NO: 1.

Sequence Notes

2. This application fails to comply with the requirements of 37 C.F.R. 1.821(d), as the specification does not provide the appropriate SEQ ID NOS: for nucleic acid and protein sequences. The specification should be amended to insert the appropriate sequence identifying (SEQ ID NO) following each recited sequence (see Appendix A and B). In addition, several minor errors were corrected by the STIC Systems Branch, which can be found on the attached sheet, "CRF Errors corrected by the STIC Systems Branch".

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-17 and 36-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-17 and 36-38 are indefinite because it is not clear as to whether the isolated nucleic acid molecule is a stress, resistance, or tolerance gene, or "portion thereof". Applicants could amend the claims to recite the elected nucleic acid, SEQ ID NO: 1, and specifically what type of gene SEQ ID NO: 1 is. Furthermore, the claims are indefinite because it is not clear as to what is meant by "portion thereof" (i.e. a portion of a stress gene or a portion of a tolerance gene or a combination of a portion of a stress and tolerance gene? It is not clear as to what constitutes a "portion thereof").

B) Claim 8 is indefinite because it is not clear as to what is meant by "hybridizes...under stringent conditions". Applicants should amend the claims to recite specific hybridization conditions.

First Paragraph-Written Description

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-17 and 36-38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

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These claims are directed to an isolated nucleic acid from *Corynebacterium glutamicum* encoding a portion of a stress, resistance, or tolerance gene of SEQ ID NO: 1. The claims are further drawn to an isolated nucleic acid sequence comprising a nucleic acid sequence that is 50% homologous to a portion of SEQ ID NO: 1, and further drawn to a nucleic acid comprising at least 15 contiguous nucleotides of SEQ ID NO: 1. The instant specification only describes the isolated nucleic acid from *Corynebacterium glutamicum* consisting of instantly claimed SEQ ID NO: 1. The specification further teaches that SEQ ID NO: 1 is a gene consisting of 1566 bp. In light of the open claim language used (i.e. a portion of a stress, resistance, or tolerance gene of SEQ ID NO: 1, 50% homology to a portion of SEQ ID NO: 1, and any fragment of at least 15 contiguous nucleotides of SEQ ID NO: 1), these claims encompass any full length sequence in which the instantly recited nucleic acids may be embedded, for example the full length genes. Therefore, it has been interpreted that the claims are inclusive of genomic sequences, including intron sequences and regulatory sequences, in addition to the full length cDNA sequence. Furthermore, the claims include language so as to include variants of the disclosed sequences with as little as 50% identity to a portion of the disclosed sequences, and any sequence which hybridizes to the disclosed sequences. Claim 7 is inclusive of sequences from other species, mutated sequences, allelic variants with functional activities distinct from that of SEQ ID NO:1, and a large genus of nucleic acids not described in the specification. However, none of these additional sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

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Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed* (See page 1117)." The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed (See Vas-Cath at page 1116)."

With the exception of SEQ ID NO: 1, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

It is noted that in Fiers v. Revel (25 USPQ2d, 1601), the Fed. Cir. concluded that "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, only the nucleic acid consisting of instant SEQ ID NO: 1 is described.

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In the application at the time of filing, there is no record or description which would demonstrate conception or written description of the isolated nucleic acid from *Corynebacterium glutamicum* encoding a **portion** of a stress, resistance, or tolerance gene of SEQ ID NO: 1, an isolated nucleic acid sequence comprising a nucleic acid sequence that is 50% homologous to a **portion** of SEQ ID NO: 1, or a nucleic acid comprising at least 15 contiguous nucleotides of SEQ ID NO: 1. Therefore, only the nucleic acid consisting of SEQ ID NO: 1, but not the full breadth of the claim meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant.

7. Claims 1-17 and 36-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid from *Corynebacterium glutamicum* consisting of instantly claimed SEQ ID NO: 1, does not reasonably provide enablement for an isolated nucleic acid from *Corynebacterium glutamicum* encoding a **portion** of a stress, resistance, or tolerance gene of SEQ ID NO: 1, an isolated nucleic acid sequence comprising a nucleic acid sequence that is 50% homologous to a **portion** of SEQ ID NO: 1, and an isolated nucleic acid comprising at least 15 contiguous nucleotides of SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The present invention is broadly drawn to an isolated nucleic acid from *Corynebacterium glutamicum* encoding a **portion** of a stress, resistance, or tolerance gene of SEQ ID NO: 1, an isolated nucleic acid sequence comprising a nucleic acid sequence that is 50% homologous to a

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portion of SEQ ID NO: 1, and a nucleic acid comprising at least 15 contiguous nucleotides of SEQ ID NO: 1.

The specification does not enable one of ordinary skill in the art to practice the invention as broadly claimed for the following reasons:

The instant specification teaches the isolated nucleic acid from *Corynebacterium glutamicum* consisting of instantly claimed SEQ ID NO: 1. The specification further teaches that SEQ ID NO: 1 is a gene consisting of 1566 bp.

Case law has established that “(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without ‘undue experimentation.’” In re Wright 990 F.2d 1557, 1561. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that “(t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art”. The amount of guidance needed to enable the invention is related to the amount of knowledge in the art as well as the predictability in the art Furthermore, the Court in Genetech Inc. v Novo Nordisk 42 USPQ2d 1001 held that “(I)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement”.

In the instant case, the claims are not commensurate in scope with the enabling disclosure because the claims are inclusive of any nucleic acid that comprises a portion of SEQ ID NO: 1, an isolated nucleic acid sequence comprising a nucleic acid sequence that is 50% homologous to a portion of SEQ ID NO: 1, and a nucleic acid comprising at least 15 contiguous nucleotides of SEQ ID NO: 1. These claims encompass any full length sequence in which the instantly recited

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nucleic acids may be embedded, for example the full length genes, genomic sequences (i.e. including intron sequences and regulatory sequences), in addition to the full length cDNA sequence, variants of the disclosed sequences with as little as 50% identity to a portion of the disclosed sequences, any sequence which hybridizes to the disclosed sequences, sequences from other species, mutated sequences, allelic variants with functional activities distinct from that of SEQ ID NO:1, and a large genus of nucleic acids not taught in the specification. The specification does not provide any guidance as to how to make and use any of these allelic variants, mutated sequences, etc. that are encompassed by the claims.

In view of the high level of unpredictability in the art and in view of the lack of specific disclosure in the specification regarding the make and use of the substantially large number of possible sequences encompassed by the claims, undue experimentation would be required to practice the invention as it is broadly claimed.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-13, 15-17 and 36-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Kunst et al. (Nature (1997) 390(6657): 249-256) and GenEmbl Accession No. Z99118).

This rejection is based on the elected nucleic acid sequence of SEQ ID NO: 1.

Kunst teaches a portion of a nucleic acid (i.e. 20 basepairs) that is 100% identical to SEQ ID NO: 1 (see GenEmbl Accession No. Z99118, sequence search result 12). Therefore, this

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sequence is at least 50% homologous to a portion of SEQ ID NO: 1 (claim 5), and would hybridize to SEQ ID NO: 1 under stringent conditions. With respect to claim 9, the reference teaches the *B. subtilis* genome, which comprises the nucleic acid of GenEmbl Accession No. Z99118 and many heterologous polypeptides (see abstract and pgs. 255-56). With respect to claims 10-13, 15-17, and 36-38, the reference teaches vectors comprising a portion of the nucleic acid of SEQ ID NO: 1, a host cell (i.e. *E. coli*) transfected with said vectors (pg. 255), and fine chemicals produced by said host cell (pg. 255).

10. Claim 6 is rejected under 35 U.S.C. 102(b) as being anticipated by Yamane (GenEmbl Accession No. AB000617).

Yamane teaches the nucleic acid which is 52.8% identical to SEQ ID NO: 1.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kunst et al. (Nature (1997) 390(6657): 249-256) and GenEmbl Accession No. Z99118), as applied to claim 1-13, 15-17 and 36-38 above, and further in view of Sinskey et al. (USPN 4,649,119).

The teachings of Kunst are presented above. Specifically, Kunst teaches a portion of a nucleic acid (i.e. 20 basepairs) that is 100% identical to SEQ ID NO: 1 (see GenEmbl Accession No. Z99118, sequence search result 12). The reference does not teach the host cell that belongs to the genus *Corynebacterium*.

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Sinsky et al. teaches the use of *Corynebacterium* as a host cell for foreign or native genes.

In view of the teachings of Sinsky et al., it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used *Corynebacterium* as a host cell, instead of *E. coli*, in order to have had an equally effective host cell for producing a fine chemical.

Conclusion

13. The prior art does not teach or suggest the isolated nucleic acid sequence from *Corynebacterium glutamicum* consisting of SEQ ID NO: 1.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (703) 305-0806. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014. Applicant is also invited to contact the TC 1600 Customer Service Hotline at (703) 308-0198.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Alexander H. Spiegler
February 7, 2002



KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

2/7/02